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13. ABSTRACT (Maximum 200 Words)

Metastatic lesions in the proximal femur are a common and serious manifestation of breast cancer. These lesions can be painful and can lead to pathological fracture. Prophylactic surgical fixation is advised in patients thought to be at high risk of fracture and typically involves placement of a prosthetic implant or compression hip screw. This study is investigating whether proximal femora with metastatic lesions can be repaired by simply filling the defect with bone cement (polymethylmethacrylate), an innovative procedure that could be performed percutaneously and could eliminate the need for implanting hardware in many cases. If defects could be repaired using this technique, patients would benefit from shorter and less invasive surgical procedures, less pain and discomfort, greatly reduced recovery time, and shorter hospital stays – all at much lower cost. To date, 423 finite element models have been created and analyzed to evaluate the effects of various defect sizes and locations on the structural capacity of proximal femora and to evaluate the effectiveness of the proposed procedure. From these data, a mathematical model has been developed to evaluate the need for prophylactic surgical fixation for specific patients. This model will form the basis of clinical guidelines for the proposed surgery.

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Introduction

Metastatic lesions in the proximal femur are a common and serious manifestation of breast cancer. These lesions can be painful and can lead to pathological fracture. Prophylactic surgical fixation is advised in those patients thought to be at high risk of fracture and typically involves placement of a prosthetic implant or a compression hip screw to provide strength. In this study, we are investigating whether proximal femora with metastatic lesions can be repaired by simply filling the defect with bone cement (polymethylmethacrylate), an innovative procedure that could be performed percutaneously and could eliminate the need for implanting hardware in many cases. If the metastatic defect could be safely repaired using this new technique, the patient would benefit from a shorter and less invasive surgical procedure, less pain and discomfort, greatly reduced recovery time, and a shorter hospital stay—all at much lower cost. Using finite element (FE) analysis, this study will also develop clinical guidelines both for assessing the need for prophylactic fixation and for using the proposed percutaneous surgical procedure. This extensive evaluation will enable rapid and safe clinical implementation of the new repair technique and surgical guidelines via a clinical trial immediately following this study.

Body

The computer programs written in Year 2 of this study [Task 2a] were used to create finite element (FE) models of proximal femora with simulated metastatic defects, allowing the effect of various defect sizes and locations to be studied. The computer programs also allowed the modeling of the drill hole that would be created when repairing these defects using the proposed percutaneous repair technique. When the FE models were used to simulate repair, the defect and drill hole were assigned the mechanical properties of bone cement (Saha, 1984).

[Task 2b] Finite element models were used to evaluate the effect of defect size and location on the structural capacity of one proximal femur before and after introduction and repair of the defect. Defect locations included the inferomedial (IM), superolateral (SL), anterior (A) and posterior (P) aspect of the femoral neck, approximately tangent to the periosteal surface at each location. To measure the effect of the defect and the subsequent repair procedure, %intact before and after percutaneous repair were respectively defined as the FE-predicted fracture load of the proximal femur before and after repair, divided by the FE-predicted fracture load of the intact model (without the defect). In order to identify "critical" defect sizes, the defect radius was increased in 0.5 mm increments at each location until %intact for the un-repaired and for the subsequent repaired models fell below 70%, indicating the smallest defect requiring prophylactic fixation and the largest that could be repaired without use of hardware, respectively.

The preliminary findings of these finite element models revealed two critical results. For defects in the SL, A, and P aspects, there did not appear to be an un-repaired defect diameter less than the anterior-posterior width of the femoral neck for which %intact was less than 70%. Defects in the IM aspect of the neck resulted in large decreases in %intact, an effect presumed due to the high stress in this region during stance-type loading conditions. Additionally, for these loading conditions, the preliminary findings indicated that there was not a critical defect size beyond which the repair technique could not be used, i.e. %intact for the repaired models always approached 100%. Hence, there does not appear to be a critical defect size beyond which the repair technique cannot be used for short term or low cyclic loading situations (i.e. for patients who are bedridden, who are wheel-chair bound, or who have short life expectancies). As a result of these findings, the defect evaluation process was modified and the study was expanded to include analysis of 12 femora (11 additional femora instead of five, as outlined in Task 2c). (A one-year no-cost extension to complete this work was requested and approved.)

In order to better evaluate the effects of defect size and location across the 12 proximal femora now included in this study, two normalized parameters were defined and measured. To obtain a normalized measure of defect size for each femur, *dd/nd* was defined as the defect diameter (*dd*) divided by the anterior-posterior neck width (*nd*) of the specific femur. Since the preliminary findings indicated that defects located on the IM aspect of the femoral neck caused the most significant decreases in femur strength, it was postulated that stress was transmitted through the cortex along this surface and the distance from the defect to the IM surface of the femur might be an appropriate measure of defect location. Therefore, *d/t* was defined as the distance from the defect to the IM surface (*d*) in a coronal section, divided by the thickness of the IM cortex (*t*). Thus, *d/t* less than 1 would indicate defect involvement of the IM cortex. In order to measure *d* with adequate repeatability, a computer program was written to calculate this distance using the CT scan data and the location of the simulated defect.

[Tasks 2c, 2d] To date, 423 FE models have been created with various combinations of *dd/nd* and *d/t*. Defects have been created with diameters of 10, 15 and 20 mm, and have been located in the IM, SL, A, and P aspects of the neck, as well as in the middle of the neck where there was no involvement of the cortex. Additionally, to measure the effect of slight changes in defect locations, defects in the IM, SL, A and P aspects of the neck were moved 1-2 mm away from the cortex, in either direction, at each location. (For defects in the A and P aspects, this did not change the value of *d*.)

The goal of these analyses is a set of guidelines that can be used clinically to evaluate the need for the proposed surgical technique for specific patients. Toward this goal, using the data collected thus far, a mathematical model has been developed to predict %intact for a patient with metastases in the femoral neck, given the measurable anatomic and tumor parameters *dd/nd* and *d/t*. ($p < 0.001$, R = 0.894).

During the upcoming one year no-cost extension, these analyses will be completed with the creation of additional FE models simulating defects of differing sizes and locations and simulating percutaneous repair of these defects. Defects will also be modeled in the subcapital region superior to the femoral neck and at the level of the lesser trochanter, two common and structurally important locations of metastatic lesions. Additionally, the fatigue strength (strength under cyclic loading) of the cement construct resulting from the proposed repair technique will be evaluated using the model results. The upcoming year will also be used for publication of our findings.

Key Research Accomplishments

- Surgical instruments and supplies needed for the proposed repair technique were identified and obtained.
- FE modeling method was calibrated to provide accurate estimates of measured fracture load.
- Measured %intact (mean = 94.7%, SD = 8.7%) clearly supports feasibility of percutaneous repair technique.
- Measured and computed fracture loads for intact and repaired femora indicate that the FE models are valid for evaluating the proposed repair technique.
- Computer programs have been developed to simulate metastatic defects and the percutaneous repair technique within the FE models.

- Feasibility of the proposed minimally invasive repair technique is indicated, at a minimum, for low cyclic loading situations.
- 423 FE models have been created and analyzed to measure the effects of various defect sizes and locations on the structural capacity of proximal femora and to determine the extent to which the proposed surgery would strengthen the proximal femur.
- A computer program has been written to allow reliable measurement of parameters required for predicting %intact, using CT scan data and the locations of simulated defects.
- The data collected thus far has been used to develop a mathematical model to predict %intact for a patient with simulated defects in the femoral neck, given measured anatomic and tumor parameters.

Reportable Outcomes

Keyak JH, Skinner HB, Kaneko TS, and Armstrong KL: Percutaneous repair of proximal femora with metastatic lesions. Department of Orthopaedic Surgery Graduate Research Forum, University of California, Irvine, CA, 5/30/03. [podium presentation]

Kaneko TK, Keyak JH: Calibration and validation of finite element models for predicting proximal femoral fracture load. Orthopaedic Research Society, 50th Annual Meeting, San Francisco, CA, 3/7-10/04. [abstract and poster presentation]

Kaneko TK, Keyak JH: Calibration and validation of finite element models for predicting proximal femoral fracture load. College of Medicine Faculty Research Poster Session, University of California, Irvine, CA, 3/24/04. [poster presentation]

Keyak JH, Kaneko TS, Skinner HB. Feasibility of a percutaneous technique for repairing proximal femora with metastatic lesions. Orthopaedic Research Society, 51st Annual Meeting, Washington, D.C., 2/20-23/05. [abstract and poster presentation]

Keyak JH, Kaneko TS, Skinner HB. Feasibility of a percutaneous technique for repairing proximal femora with metastatic lesions. Skeletal Complications of Malignancy IV, Bethesda, MD, 4/28-30/05. [abstract and poster presentation]

Keyak JH, Kaneko TS, Rossi SA, Pejcic MR, Tehranzadeh J, Skinner HB. Predicting the strength of femoral shafts with and without metastatic lesions. Clin Orthop Rel Res (in press).

Keyak JH, Kaneko TS, Tehranzadeh J, Skinner HB. Predicting proximal femoral strength using structural engineering models. Clin Orthop Rel Res (in press).

Conclusions

Conventional surgery to prevent pathological fracture, involving implantation of hardware, is invasive. If a metastatic defect can be safely repaired percutaneously by simply filling the defect with bone cement, <u>the patient would benefit from a shorter and less invasive surgical procedure with less pain and discomfort, greatly reduced recovery time, and shorter hospital stay – all at much lower cost.</u>

The decision to perform prophylactic fixation is complicated by the inadequacy of tools for identifying patients in need of fixation (Hipp et al., 1995). This study is addressing this issue by providing surgical guidelines based on the size and location of the lesion. More significantly, this study will establish a minimally-invasive alternative to traditional surgical fixation that will reduce the reluctance to perform surgical repair in those cases where the need for intervention is unclear.

Results to date indicate that the proposed minimally invasive procedure is a viable option for, at a minimum, situations with low cyclic loading, such as for patients who are bedridden, who are wheel chair bound, or who have short life expectancies. Data from 423 finite element models have been used to develop a mathematical model to evaluate the need for surgical intervention for specific patients. This model will form the basis of clinical guidelines for the proposed surgery.

References

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Saha S, Pal S: Mechanical properties of bone cement: a review. J Biomed Mat Res 18:435-462, 1984.